Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

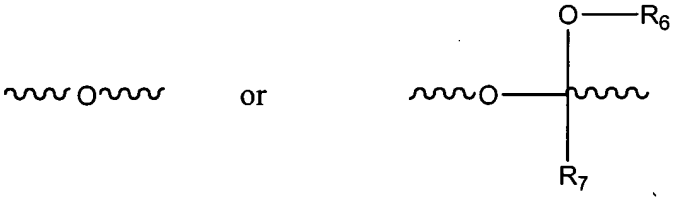
Listing of Claims:

1. (Original) A protected anti-neoplastic agent of the formula Hyp-L-N or Hyp-N, wherein

Hyp is a hypoxic activator;

N is an anti-neoplastic agent; and

L is a linking group of the formula  , where X is selected from



where R_6 is unsubstituted alkyl or alkyl substituted with one or more heteroatom containing groups;

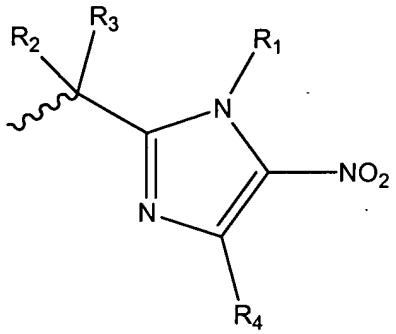
R_7 is hydrogen, unsubstituted alkyl or alkyl substituted with one or more heteroatom containing groups; and

Y is a spacer group selected from a substituted or unsubstituted $-(CH_2)_n-$ chain with n=1-4; a substituted or unsubstituted $-(CH_2)_n-$ chain with n=1-4 in which one of the carbon backbone chain atoms is substituted by a heteroatom containing group; and a delayed release group comprising an aromatic group.

2. (Original) The protected anti-neoplastic agent of claim 1, wherein the hypoxic activator is selected from the group consisting of electron deficient nitrobenzene moieties, electron deficient nitrobenzoic acid amide moieties, nitroazole moieties, nitroimidazole moieties, nitrothiophene moieties, nitrothiazole moieties, nitrooxazole moieties, nitrofuran moieties, and nitropyrrole moieties.

3. (Original) The protected anti-neoplastic agent of claim 2, wherein the hypoxic activator is a substituted or unsubstituted nitroimidazole moiety.

4. (Original) The protected anti-neoplastic agent of claim 3, wherein the hypoxic activator is a moiety of the formula



wherein

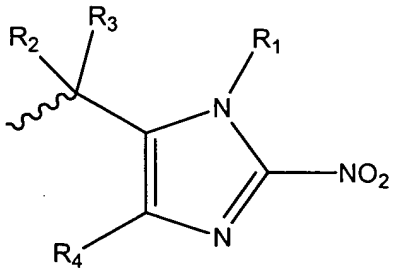
R_2 is hydrogen;

R_3 is hydrogen or C_1-C_6 alkyl;

R_1 is an electron withdrawing group, an unsubstituted C_1-C_6 alkyl, C_1-C_6 alkyl substituted with one or more heteroatom-containing groups, unsubstituted C_1-C_6 alkoxy, or C_1-C_6 alkoxy substituted with one or more heteroatom-containing groups; and

R_4 is an electron withdrawing group, -H, unsubstituted C_1-C_6 alkyl, C_1-C_6 alkyl substituted with one or more heteroatom-containing groups, unsubstituted C_1-C_6 alkoxy, or C_1-C_6 alkoxy substituted with one or more heteroatom-containing groups.

5. (Original) The protected anti-neoplastic agent of claim 3, wherein the hypoxic activator is a moiety of the formula



wherein

R_2 is hydrogen;

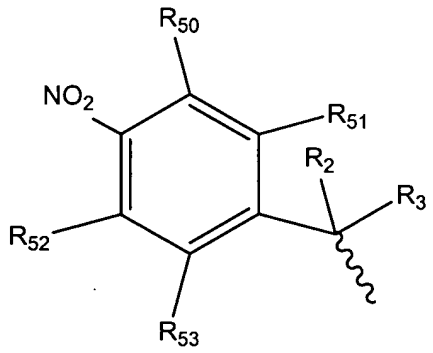
R_3 is hydrogen or C_1-C_6 alkyl;

R_1 is unsubstituted C_1-C_6 alkyl, C_1-C_6 alkyl substituted with one or more heteroatom-containing groups, unsubstituted C_1-C_6 alkoxy, or C_1-C_6 alkoxy substituted with one or more heteroatom-containing groups; and

R_4 is -H, unsubstituted C_1-C_6 alkyl, C_1-C_6 alkyl substituted with one or more heteroatom-containing groups, unsubstituted C_1-C_6 alkoxy, or C_1-C_6 alkoxy substituted with one or more heteroatom-containing groups.

Claims 6-16 (Cancelled).

17. (Original) The protected anti-neoplastic agent of claim 2, wherein the hypoxic activator is a nitrobenzene of formula



where

R_2 is hydrogen;

R_3 is -H, C_1-C_6 alkyl; and

R_{50} , R_{51} , R_{52} , and R_{53} are independently selected from an electron withdrawing group, H, C_{1-6} alkyl or C_{1-6} alkoxy; where the alkyl and alkoxy are optionally independently substituted with one or more groups selected from ether (-OR^{20}), amino (-NH_2), mono-substituted amino (-$NR^{20}H$), di-substituted amino (-$NR^{21}R^{22}$), cyclic C_{1-5} alkylamino, imidazolyl, C_{1-6} alkylpiperazinyl, morpholino, thiol (-SH), thioether -(SR^{20}), tetrazole, carboxylic acid (-

COOH), ester (-$COOR^{20}$), amide (-$CONH_2$), mono-substituted amide (-$CONHR^{20}$), disubstituted amide (-$CONR^{21}R^{22}$), N-connected amide (-NH_2-C(=O)-R^{20}), mono-substituted N-connected amide (-NHR^{21}-C(=O)-R^{20}), disubstituted N-connected amide (-$NR^{21}R^{22}$-$S(=O)_2$-R^{20}), N-connected sulfonamide (-NH_2-$S(=O)_2$-R^{20}), mono-substituted N-connected sulfonamide (-NHR^{21}-$S(=O)_2$-R^{20}), disubstituted N-connected sulfonamide (-$NR^{21}R^{22}$-$S(=O)_2$-R^{20}), sulphoxy (-$S(=O)_2OH$), sulphonate ($S(=O)_2OR^{20}$), sulphonyl ($S(=O)_2R^{20}$), sulphixy (S(=O)OH), sulphinate ($S(=O)OR^{20}$), sulphinyl ($S(=O)R^{20}$), phosphonooxy ($OP(=O)(OH)_2$), phosphate ($OP(=O)(OR^{20})_2$), and sulfonamide (-$S(=O)_2NH_2$, -$S(=O)_2NHR^{21}$, or -$S(=O)_2NR^{21}R^{22}$), where R^{20}, R^{21}, and R^{22} are independently selected from a C_1-C_6 alkyl group; and wherein the electron withdrawing group is selected from halo, cyano (-CN), haloalkyl, carboxamide, nitro, aldehydo (-CHO), keto (-COR^{20}), alkenyl, alkynyl, quaternary amino (-$N^+R^{20}R^{21}R^{22}$), ester (-$COOR^{20}$), amide (-$CONH_2$), mono-substituted amide (-$CONHR^{20}$), disubstituted amide (-$CONR^{21}R^{22}$), N-connected amide (-NH_2-C(=O)-R^{20}), mono-substituted N-connected amide (-NHR^{21}-C(=O)-R^{20}), disubstituted N-connected amide (-$NR^{21}R^{22}$-$S(=O)_2$-R^{20}), N-connected sulfonamide (-NH_2-$S(=O)_2$-R^{20}), mono-substituted N-connected sulfonamide (-NHR^{21}-$S(=O)_2$-R^{20}), disubstituted N-connected sulfonamide (-$NR^{21}R^{22}$-$S(=O)_2$-R^{20}), sulphoxy (-$S(=O)_2OH$), sulphonate ($S(=O)_2OR^{20}$), sulphonyl ($S(=O)_2R^{20}$), and sulfonamide (-$S(=O)_2NH_2$, -$S(=O)_2NHR^{21}$, or -$S(=O)_2NR^{21}R^{22}$), where R^{20}, R^{21}, and R^{22} are independently a C_1-C_6 alkyl group.

18. (Original) The protected anti-neoplastic agent of claim 1, wherein the anti-neoplastic agent is bonded to the hypoxic activator (Hyp) or linking group (L) through an -O- or -NR_5- group in the anti-neoplastic agent, where R_5 is -H, or C_1-C_6 alkyl, optionally substituted with one or more groups selected from hydroxyl, ether, thiol, thioether, sulfinic ester, sulfoxide, sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide , aldehydo, keto, amino, halo, and cyano.

19. (Original) The protected anti-neoplastic agent of claim 1, wherein the anti-neoplastic agent is selected from the group consisting of doxorubicin, daunorubicin, duocarmycin, etoposide, duetoposide, Combretastatin A-4, vinblastine, vincristine, camptothecin, topotecan, 5-fluorouracil, AQ4N, hydroxyurea, maytansines, enediyenes,

discodermolides, epothilones, taxanes, calicheamicins, tedanolides, bleomycins, calicheamicins, colchicine, cytarabine, dacarbazine, dactinomycin, discodermolides, epirubicin, epirubicin derivatives, fludarabine, hydroxyureapentostatin, 6-mercaptopurine, methotrexate, mitomycin, mitoxantrone, carboplatin, cisplatin, prednisone, procarbazine, taxanes, docetaxel, paclitaxel, tedanolides, teniposide, 6-thioguanine, vinca alkaloids, cyclophosphamides, platinum coordination complexes, anthracenediones, substituted ureas, and methylhydrazine derivatives.

Claim 20 (Cancelled).

21. (Original) The protected anti-neoplastic agent of claim 1, wherein the compound released upon reduction of the hypoxic activator has an IC_{50} of less than about 100nM.

22. (Original) The protected anti-neoplastic agent of claim 1, wherein the anti-neoplastic agent is bonded to the hypoxic activator (Hyp) or linking group (L) by an -O- group in the anti-neoplastic agent, and wherein the -O- group is bonded to an aromatic group in the anti-neoplastic agent.

Claim 23 (Cancelled).

24. (Original) The protected anti-neoplastic agent of claim 1, wherein

R_6 is unsubstituted C_1-C_{10} alkyl or C_1-C_{10} alkyl substituted with one or more heteroatom containing groups selected from hydroxyl, ether, thiol, thioether, sulfinic ester, sulfoxide, sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide , aldehydo, keto, amino, halo, and cyano; and

R_7 is hydrogen, unsubstituted C_1-C_{10} alkyl, or C_1-C_{10} alkyl substituted with one or more heteroatom containing groups selected from hydroxyl, ether, thiol, thioether, sulfinic ester, sulfoxide, sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide , aldehydo, keto, amino, halo, and cyano.

Claim 25 (Cancelled).

26. (Original) The protected anti-neoplastic agent of claim 1, wherein R_6 is unsubstituted C_1-C_{10} alkyl; and R_7 is hydrogen or unsubstituted C_1-C_{10} alkyl.

Claims 27-28 (Cancelled).

29. (Original) The protected anti-neoplastic agent of claim 1, wherein the spacer group Y is an unsubstituted -$(CH_2)_n$- chain with n=1-4, or a -$(CH_2)_n$- chain with n=1-4 substituted with one or more heteroatom containing groups selected from hydroxyl, ether, thiol, thioether, sulfinic ester, sulfoxide, sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide , aldehydo, keto, amino, halo, and cyano.

Claims 30-38 (Cancelled).

39. (Original) The protected anti-neoplastic agent of claim 1, wherein X is the acetal group and Y is -(CR^eR^f)-R^m-(CR^jR^k)-(CH_2)-, where R^e, R^f are independently hydrogen, unsubstituted C_1-C_3 alkyl, C_1-C_3 alkyl substituted with one or more of hydroxyl, ether, thiol, thioether, sulfinic ester, sulfoxide, sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide , aldehydo, keto, amino, halo, and cyano, or (CR^eR^f) is (C=O); R^j and R^k are independently hydrogen, unsubstituted C_1-C_3 alkyl, C_1-C_3 alkyl substituted with one or more of hydroxyl, ether, thiol, thioether, sulfinic ester, sulfoxide, sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide , aldehydo, keto, amino, halo, and cyano, or (CR^jR^k) is (C=O); and R^m is selected from –O-, -S-, -$S(=O)_{2-}$, and –NR^{30}-, where R_{30} is selected from –$C(=O)R^{31}$, -$C(=O)NR^{31}R^{32}$, -H, C_1-C_{10} alkyl or C_1-C_{10} alkyl substituted with one or more heteroatom containing groups selected from hydroxyl, ether, thiol, thioether, sulfinic ester, sulfoxide, sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide , aldehydo, keto, amino, halo, and cyano; and R^{31} and R^{32} are independently selected from C_1-C_{10} alkyl or C_1-C_{10} alkyl substituted with one or more heteroatom containing groups, selected from hydroxyl, ether, thiol, thioether, sulfinic ester,

sulfoxide, sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide , aldehydo, keto, amino, halo, and cyano.

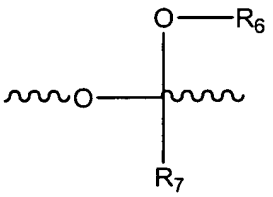
Claim 40 (Cancelled).

41. (Original) The protected anti-neoplastic agent of claim 1, wherein Y is the delayed release group and has the formula $\sim\sim R_{10}—R_{11}—R_{12}\sim\sim$ where R_{10} is a bond ; R_{11} is an unsubstituted or substituted aryl or heteroaryl group; and R_{12} has the formula $-(CR^{40}R^{41})-R^{42}-$ or $-(CR^{40}R^{41})-CR^{43}=CR^{44}-R^{42}-$, where R^{42} is a bond or -OC(=O)-, and R^{40}, R^{41}, R^{42}, and R^{43} are independently selected from -H, unsubstituted C_1-C_{10} alkyl, and C_1-C_{10} alkyl substituted with one or more heteroatom containing groups selected from hydroxyl, ether, thiol, thioether, sulfinic ester, sulfoxide, sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide , aldehydo, keto, amino, halo, and cyano.

Claims 42-52 (Cancelled).

53. (Original) A protected anti-neoplastic agent, in which the anti-neoplastic agent includes one or more protectable hydroxyl groups or amine groups, and wherein one or more of the protectable hydroxyl groups or amine groups is substituted with a group selected from Hyp-L- or Hyp-, wherein Hyp is a hypoxic activator; and L is a linking group of the formula $\sim\sim X—Y\sim\sim$, where X is selected from

and



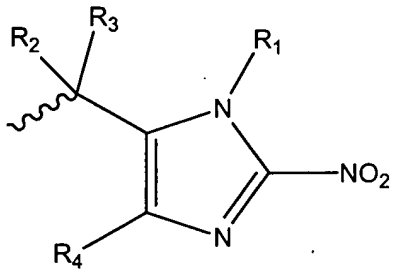
where R_6 is unsubstituted alkyl or alkyl substituted with one or more heteroatom containing groups;

R_7 is hydrogen, unsubstituted alkyl or alkyl substituted with one or more heteroatom containing groups; and

Y is a spacer group selected from a substituted or unsubstituted -$(CH_2)_n$- chain with n=1-4; a substituted or unsubstituted -$(CH_2)_n$- chain with n=1-4 in which one of the carbon backbone chain atoms is substituted by a heteroatom containing group; and a delayed release group comprising an aromatic group.

54. (Original) The protected anti-neoplastic agent of claim 53, wherein the hypoxic activator is selected from the group consisting of electron deficient nitrobenzene moieties, electron deficient nitrobenzoic acid amide moieties, nitroazole moieties, nitroimidazole moieties, nitrothiophene moieties, nitrothiazole moieties, nitrooxazole moieties, and nitrofuran moieties, and nitropyrrole moieties.

55. (Original) The protected anti-neoplastic agent of claim 54, wherein the hypoxic activator is a nitroimidazole of the formula



wherein

R_2 is hydrogen;

R3 is -H or C1-C6 alkyl;

R1 is substituted or unsubstituted C1-C6 alkyl or substituted or unsubstituted C1-C6 alkoxy; and

R4 is -H, substituted or unsubstituted C1-C6 alkyl, or substituted or unsubstituted C1-C6 alkoxy;

wherein the R1 and R4 substituted alkyl and substituted alkoxy are independently substituted with one or more heteroatom-containing groups selected from ether (-OR20), amino

(-NH2), mono-substituted amino (-NR20H), di-substituted amino (-NR21R22), cyclic C1-5 alkylamino, imidazolyl, C1-6 alkylpiperazinyl, morpholino, thiol (-SH), thioether -(SR20), tetrazole, carboxylic acid (-COOH), ester ($-COOR^{20}$), amide ($-CONH_2$), mono-substituted amide ($-CONHR^{20}$), disubstituted amide ($-CONR^{21}R^{22}$), N-connected amide ($-NH_2-C(=O)-R^{20}$), mono-substituted N-connected amide ($-NHR^{21}-C(=O)-R^{20}$), disubstituted N-connected amide ($-NR^{21}R^{22}-S(=O)_2-R^{20}$), N-connected sulfonamide ($-NH_2-S(=O)_2-R^{20}$), mono-substituted N-connected sulfonamide ($-NHR^{21}-S(=O)_2-R^{20}$), disubstituted N-connected sulfonamide ($-NR^{21}R^{22}-S(=O)_2-R^{20}$), sulphoxy ($-S(=O)_2OH$), sulphonate ($S(=O)_2OR^{20}$), sulphonyl ($S(=O)_2R^{20}$), sulphixy (S(=O)OH), sulphinate ($S(=O)OR^{20}$), sulphinyl ($S(=O)R^{20}$), phosphonooxy ($OP(=O)(OH)_2$), phosphate ($OP(=O)(OR^{20})_2$), and sulfonamide ($-S(=O)_2NH_2$, $-S(=O)_2NHR^{21}$, or $-S(=O)_2NR^{21}R^{22}$), where R^{20}, R^{21}, and R^{22} are independently selected from a C_1-C_6 alkyl group; and

L is a linking group of the formula ~~~X——Y~~~ , where X is selected from

R6 is unsubstituted C1-C3 alkyl or C1-C3 alkyl substituted with one or more heteroatom containing groups selected from hydroxyl, ether, thiol, thioether, sulfinic ester, sulfoxide, sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide , aldehydo, keto, amino, halo, and cyano;

R7 is hydrogen, unsubstituted C1-C3 alkyl, or C1-C3 alkyl substituted with one or more heteroatom containing groups selected from hydroxyl, ether, thiol, thioether, sulfinic ester, sulfoxide, sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide , aldehydo, keto, amino, halo, and cyano; and

the spacer group Y is an unsubstituted $-(CH_2)_n-$ chain with n=1-4, or a $-(CH_2)_n-$ chain with n=1-4 substituted with one or more heteroatom containing groups selected from hydroxyl, ether, thiol, thioether, sulfinic ester, sulfoxide, sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide , aldehydo, keto, amino, halo, and cyano; or

the spacer group Y is the delayed release group and has the formula ~~~R_{10}—R_{11}—R_{12}~~~ where R10 is a bond ; R11 is an unsubstituted or substituted aryl or substituted or unsubstituted heteroaryl group; and R12 has the formula –(CR40R41)-R42- or –

(CR40R41)-CR43=CR44-R42- , where R42 is a bond or -OC(=O)-, and R40, R41, R42, and R43 are independently selected from -H, unsubstituted C1-C10 alkyl, and C1-C10 alkyl substituted with one or more heteroatom containing groups selected from hydroxyl, ether, thiol, thioether, sulfinic ester, sulfoxide, sulfone, sulfonic acid, sulfonic acid ester, sulfenamide, sulfonamide, carboxylic acid, carboxylic acid salt, ester, amide , aldehydo, keto, amino, halo, and cyano.

Claims 56-63 (Cancelled).

64. (Currently amended): A method for treating cancer comprising administering to a subject a therapeutically effective amount of a protected anti-neoplastic agent according to claim 1 ~~any of claims 1 and 53~~.

Claims 65-87 (Cancelled).

88. (New): A method for treating cancer comprising administering to a subject a therapeutically effective amount of a protected anti-neoplastic agent according to claim 53.